

Atty Dkt. No.: AREN-001CIP  
USSN: 09/060,188

**AMENDMENTS TO THE CLAIMS:**

Please incorporate the following amendments into the claims of the subject application.

1-33. (canceled)

34. (previously presented) The method of claim 69 wherein the compound is determined to be a compound that reduces the activity of an active receptor state of said constitutively activated GPCR.

35-39. (canceled)

40. (previously presented) The method of claim 70 wherein the compound is determined to be a compound that reduces the activity of an active receptor state of said constitutively active GPCR.

41-44. (canceled)

45. (currently amended) The method of claim 69 wherein the third intracellular loop of the endogenous GPCR of step (a) comprises the following sequence:

X1BBHyX2

Wherein wherein X1 is an amino acid; B is a basic amino acid; Hy is a hydrophobic amino acid; and X2 is an amino acid.

46. (original) The method of claim 45 wherein X1 is glycine.

47. (original) The method of claim 45 wherein X1 is lysine.

48. (original) The method of claim 45 wherein Hy is alanine.

49. (original) The method of claim 45 wherein X2 is lysine.

50. (original) The method of claim 45 wherein X2 is arginine.

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51. (original) The method of claim 45 wherein X2 is glutamic acid.

52. (previously presented) The method of claim 69 wherein the second intracellular loop of the endogenous GPCR of step (a) comprises the following sequence:

XRY

wherein X can be any amino acid other than aspartic acid; R is arginine; and Y is tyrosine.

53. (previously presented) The method of claim 70 wherein the third intracellular loop of the constitutively active GPCR of step (a) comprises the following sequence:

X1BBHyX2

wherein X1 is an amino acid; B is a basic amino acid; Hy is a hydrophobic amino acid; and X2 is an amino acid.

54. (original) The method of claim 53 wherein X1 is glycine.

55. (original) The method of claim 53 wherein X1 is lysine.

56. (original) The method of claim 53 wherein Hy is alanine.

57. (original) The method of claim 53 wherein X2 is lysine.

58. (original) The method of claim 53 wherein X2 is arginine.

59. (original) The method of claim 53 wherein X2 is glutamic acid.

60. (previously presented) The method of claim 70 wherein the second intracellular loop of the constitutively active GPCR of step (a) comprises the following sequence:

XRY

wherein X can be any amino acid other than aspartic acid; R is arginine; and Y is tyrosine.

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61. (original) The method of claim 45 wherein the sequence XIBBH<sub>y</sub>X2 is an endogenous sequence.

62. (original) The method of claim 52 wherein the sequence XRY is an endogenous sequence.

63. (currently amended) The method of claim 69 wherein ~~said mammalian tissue source~~  
mammal is a ~~human-tissue source~~.

64. (currently amended) The method of claim 70 wherein ~~said mammalian tissue source~~  
mammal is a ~~human-tissue source~~.

65. (currently amended) The method of claim 69 wherein ~~said mammalian tissue source~~  
mammal is a ~~non-human-tissue source~~ mammal.

66. (currently amended) The method of claim 70 wherein ~~said mammalian tissue source~~  
mammal is a ~~non-human-tissue source~~ mammal.

67. (canceled)

68. (canceled)

69. (currently amended) A method for directly identifying a non-endogenous candidate compound as a compound that stimulates an endogenous G protein coupled receptor (GPCR) or reduces the activity of an active receptor state of an endogenous GPCR, wherein said endogenous GPCR has been associated with a disease or disorder in a mammal and wherein an endogenous ligand for said endogenous GPCR has not been identified, said method comprising the steps of:

- (a) subjecting said endogenous GPCR to constitutive receptor activation to create a constitutively activated GPCR;
- (b) contacting the non-endogenous candidate compound with said constitutively activated GPCR;

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(c) determining whether said non-endogenous candidate compound is a compound that stimulates said endogenous GPCR or reduces the activity of an active receptor state of said endogenous GPCR, by measuring the ability of the compound to stimulate or inhibit functionality of said constitutively activated GPCR, respectively.

70. (currently amended) A method for directly identifying a non-endogenous candidate compound as a compound that stimulates an endogenous constitutively active G protein coupled receptor (GPCR) or reduces the activity of an active receptor state of an endogenous constitutively active GPCR, wherein said endogenous GPCR has been associated with a disease or disorder in a mammal and wherein an endogenous ligand for said constitutively active GPCR has not been identified, said method comprising the steps of:

(a) contacting the non-endogenous candidate compound with said constitutively active GPCR;  
(b) determining by measurement of the ability of the compound to inhibit or stimulate functionality of said constitutively active GPCR, whether said non-endogenous candidate compound is a compound that stimulates said constitutively active GPCR or reduces the activity of an active receptor state of said constitutively active GPCR.

71. (withdrawn) A compound directly identified by the method of claim 69.

72. (withdrawn) A compound directly identified by the method of claim 70.

73. (withdrawn) A pharmaceutical composition comprising the compound of claim 71.

74. (withdrawn) A pharmaceutical composition comprising the compound of claim 72.

75-76. (canceled)